

Plasma Cytokine Levels During Long-Duration Spaceflight

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Background: We monitored the plasma concentrations of 22 cytokines and chemokines in 17 astronauts during long-duration spaceflight onboard the International Space Station. Plasma cytokine concentration may serve as an indicator of *in-vivo* immune responses. Cytokines may be subdivided into several categories, allowing monitoring of different types of biological responses. These include innate immunity pro-inflammatory, anti-inflammatory, adaptive immunity T cell biases (Th1, Th17, Th2), growth factors and chemokines. There is also some category overlap for specific cytokines. In general, cytokines possess a short half-life, and are locally acting. Therefore, the plasma level for most cytokines are extremely low. Exceptions include some chemokines, which due to their role in leukocyte trafficking and recruitment must leave a localized site of inflammation and persist in the general circulation. Blood samples were collected twice before flight, 3-5 times during flight (depending on mission duration), at landing and 30 days post-landing.

Results: With some exceptions, there were no detectable levels of innate inflammatory cytokines (IL-1a, IL-1b, TNFa, IL-6), nor adaptive immunity cytokines (IL-2, IFNg, IL-17, IL-4, IL-5, IL-10) at any flight phase. This is consistent with generally healthy crews, limited incidence of infectious disease and previous reports of diminished T cell function during spaceflight. Despite the lack of changes in mean innate inflammatory cytokines during spaceflight, there was considerable variation in individual crew responses. In-flight plasma TNFa was significantly correlated with 3-methylhistidine, a marker of muscle catabolism ($P < 0.05$), and estimates of body iron stores ($P < 0.05$). The anti-inflammatory cytokine IL-1ra is constitutively present in plasma, and the concentration was significantly elevated during the first few weeks of spaceflight ($P < 0.03$). IL-8 levels were also significantly elevated during spaceflight. The growth factors Tpo and VEGF are constitutively present in plasma, and levels of both were significantly elevated during spaceflight. For other growth factors (G-CSF, GM-CSF, FGFbasic) levels were minimal and generally unchanged during flight. Some chemokines are constitutively present in plasma. CXCL5 is constitutively present in plasma at high concentration and was significantly increased during spaceflight. CCL4 was also increased, more predominantly during the early mission phase. CCL2 and RANTES are constitutively present in plasma, however there were no alterations observed during spaceflight.

Conclusion: Reduced T cell, granulocyte, NK and monocyte function have all been reported following both long and short duration spaceflight, however these data indicate crews are generally not experiencing inflammatory or adaptive immune activation during spaceflight. There appear to be varied individual crew responses, and specific relationships between cytokines and markers of iron status and muscle turnover that warrant further evaluation. Increases in growth factors and chemokines may indicate other types of adaptation occurring during spaceflight, such as attempts to overcome diminished immunocyte function.